Type II Ribosome Inactivating Proteins (RIPs), commonly known as A/B toxins are heterodimers comprising of a catalytically active A chain, an RNA N-glycosidase which inhibits protein synthesis and a lectin-like B chain required for the binding of the toxin to the cell surface and internalization of the same. Abrin is a type II RIP obtained from the mature seeds of *Abrus precatorius* plant that is extremely toxic and has been shown to be 75 times more potent than its well studied sister toxin, ricin. The LD_{50} dose for abrin is only 2.8 µg/kg body weight of mice and its potential use in bio-warfare is a cause of major concern. Abrin has been classified as a select agent by the Centre for Disease Control and Prevention, U.S.A., because it is stable, effective at very low concentrations and easy to purify and disseminate in large amounts. In spite of abrin being a potential bio-warfare agent, there is no antidote or vaccine available against this toxin till date. The first and only neutralizing monoclonal antibody (mAb) against abrin, namely D6F10, was reported from our laboratory and has been shown to rescue toxicity of abrin in cells as well as in mice. The study reported in the thesis focuses on understanding the mechanism of neutralization of abrin by the mAb D6F10 and development of a potential vaccine candidate against the toxin.

In order to map the epitope corresponding to the antibody, first, overlapping gene deletion constructs spanning the entire length, 251 amino acids, of ABA were generated and checked for binding to the mAb. Fragments shorter than 1-175 did not show immuoreactivity. Analysis of the crystal structure of abrin A chain revealed that a helix spanning the amino acids 148-167 was present at the core of the protein structure and truncation in this region of the protein possibly results in loss of conformation leading to abrogation of antibody binding. Therefore, a novel strategy of epitope mapping was adopted. *Abrus precatorius* agglutinin (APA) is a homologue of abrin obtained from the same plant source. The A chains of abrin and APA share 67% sequence identity and their crystal structures superimpose very well but unlike abrin the APA A chain does not bind the mAb D6F10. Chimeric constructs were generated within the region 1-175 of A chains of both ABA and APA and deletions and mutations of the ABA was then made on the APA as scaffold. It could be concluded that the amino acids of the region 75123 are involved in the formation of the epitope. Further, based on sequence alignment of ABA and APA A chain 13 residues in the chimera $ABA_{1\text{-}123}APA_{124\text{-}175}$ were mutated and it was found that the mutation of the residues Thr 112, Gly 114 and Arg 118 resulted in loss of binding to the antibody. Furthermore, the mAb D6F10 rescues inhibition of protein synthesis by abrin in HeLa cells by internalizing in cells along with abrin and possibly occluding the active site cleft of ABA. The antibody prevents cell attachment of abrin at higher concentrations. The observations provide novel insights into mechanisms of many known neutralizing antibodies against A/B toxins. The study also highlights that chimeric protein constructs could possibly be developed as potential vaccine candidates for neutralization of abrin intoxication.